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REMARKS

Status of the Claims

Claims 47, 58, 59, 61, 67-69, 71-73 and 115-119 are pending in the application. Claims 47, 58, 59, 61, 67-69, 71-73 and 115-119 are rejected.

Claim 47 is amended and claim 61 is canceled herein. No new matter is added to the amended claim.

Claim Amendments

Claim 47 is amended by incorporating the limitation of canceled claim 61. Amended claim 47 is directed to a method for inducing death in cancer cells. This method comprises injecting an adenoviral vector encoding a Fas ligand into cancer cells that express a Fas receptor. The adenoviral vector used in this method comprises a tissue specific promoter and an inducible promoter or an inducible promoter to control the expression of the Fas ligand. Injection of such an adenoviral vector results in the expression of the Fas ligand in the cancer cells, which further leads to induction of apoptosis through specific binding with the Fas receptor expressed therein.

The 35 U.S.C. §112, First paragraph , Rejection

Claims 118 and 119 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Applicant respectfully traverses this rejection.

The Examiner maintains that since each claim is directed to a specific vector, each claim is defined by a specific sequence that would correspond to each of the vector. In the absence of such a sequence, a single nucleotide change would distinguish vectors that otherwise have the requisite structural elements (e.g. tet-responsive element, GFP, FasL). Hence, the Examiner maintains that the vectors recited in the claims 118 and 119 must be deposited.

Applicant respectfully disagrees with the Examiner. In general, the novel and inventive concept of the claimed invention is that the vector used in the claimed method is a double recombinant adenoviral vector with the tet-responsive element and the transactivator element built into the opposite ends of the same vector (page 25, lines 14-17; fig. 1C). More specifically, the instant invention is drawn to Ad/FasL-GFP$_{TET}$ in which the FasL-GFP fusion protein is expressed from TRE promoter. The TRE-controlled FasL-GFP fusion gene and the transactivator element are placed in the opposite ends of the same vector (page 30, lines 1-23).

With regards to constructing the claimed vectors, Applicant reiterates that the method of constructing fusion proteins and the sequence of murine FasL is known in the art. What is important, however, is the length of the FasL that is fused with GFP protein. The instant specification teaches that DNA encoding 11 to 279 amino acids of the murine FasL was placed downstream of the GFP sequence present in a commercially available vector. The instant specification further teaches that all the vectors used to construct the claimed

vectors were commercially available. Hence, the maps of these vectors are also known. The specification and the figures of the instant invention provide further guidance as to the arrangement of the genes in the vector with reference to the restriction sites and the length of the gene sequence within the vector (page 26, lines 16-26; Figs. 1A-1C). Since construction of vectors is routine in the art, Applicant contends that based on the guidance provided in the specification and figures, one of ordinary skill in the art will be able to construct an adenoviral vector with the tet-responsive element and the transactivator element built into the opposite ends of the same vector. Hence, Applicant contends that the instant specification provides ample guidance to one of ordinary skill in the art to arrive at the claimed vectors. Accordingly, based on the above-mentioned remarks, Applicant respectfully requests that the rejection of claims 118 and 119 under 35 U.S.C §112, first paragraph be withdrawn.

Claims 47, 58-59, 61, 67-69, 71-73 and 115-119 stand rejected under 35 U.S.C. §112, first paragraph, for lack of enablement for *in vivo* use. Applicant respectfully traverses this rejection.

The Examiner has maintained the rejection of these claims since neither Applicant's amendments nor arguments submitted in response to this rejection in the last Final Office Action were found persuasive. The Examiner provides lack of support for systemic administration of vectors in the instant specification and in the Declaration provided by the Applicant and unpredictability in the art for in vivo use of adenoviral vectors as reasons for rejecting claim 47.

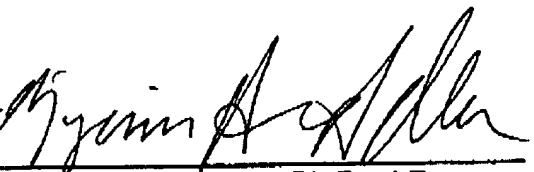
Applicant has amended claim 47 as discussed supra. The instant specification teaches a method of treating a tumor containing cells that express Fas by introducing a nucleic acid encoding a Fas ligand (FasL) into a second tumor cell using the vector described *supra*, whereby this second tumor cell expresses FasL and interacts with the Fas^+ tumor cell to cause the apoptosis of the Fas^+ cell (page 6, line 29-page 7, line 5). It further teaches the bystander effect induced by the claimed method in prostatic adenocarcinoma where these prostate cancer cells undergo apoptosis through a paracrine/autocrine mechanism (Example 3). Thus, the method discussed therein not only ensures that all the cells within that tumor undergo apoptosis but that the apoptotic effect will be localized to the tumor and not affect surrounding normal cells.

Furthermore, the instant specification teaches that the claimed virus could be administered without lethality and resulted in tumor cell growth retardation *in vivo* (page 37, lines 3-11). Despite this, should the virus leak out of the tumor and a systemic toxic effect is detected, the instant specification teaches shutting off the virus by either downregulating or upregulating the inducible promoter (page 37, lines 15-27). Thus, Applicant submits that the teachings of the instant specification provides evidence of efficacy of the method claimed in amended claim 47. Applicant also contends that the claimed invention provides ample guidance for one skilled in the art to practice the invention *in vivo*. Accordingly, based on the above-mentioned remarks, Applicant respectfully requests the withdrawal of rejection of claims 47, 58-59, 61, 67-69, 71-73 and 115-119 under 35 U.S.C. 112, first paragraph.

This is intended to be a complete response to the Final Office Action mailed February 03, 2006. Applicants submit that the pending claims are in condition for allowance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution. Applicant also encloses a Request for Continued Examination and a petition to extend the time for filing this response for three (3) months to and including August 3, 2006. Please charge the $510 extension fee to the credit card identified on the enclosed PTO-2038. In the absence of this form, please debit the fees due from Deposit Account No. 07-1185 on which Applicant's counsel is allowed to draw.

Respectfully submitted,

Date: 8/1/06



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